Remarks/Arguments

In response to the Rejection mailed March 18, 2004, Applicants have amended the specification, canceled claims 4, 9 13-55, amended claims 1, 2, 3, 6, 7, 8, 11, and 12, added new claims 56-68 and present the following remarks.

Claims 7 and 8 were objected to for the phraseology of the P value. These claims have been amended as suggested by the examiner.

The specification has been objected to for reciting "not prior art" in the background in section of the specification. The passage and associated reference were deleted. The specification is also objected as listing Accession numbers in the tables without indicating the source of the Accession numbers. The source for the accession numbers is given on page 14 last sentence.

The Oath/Declaration was objected to as omitting the mailing address of each inventor. Attached is an application data sheet providing that information.

The title was objected to as not being descriptive. The elected claims include protein disease markers and thus the title is proper. Nonetheless, a new title is provided.

Claims 1-12 were rejected under 35 USC 112, first paragraph as not being enabling for all diseases. The claims have been amended to recite determining one of 5 conditions. It will be appreciated that some diseases are inadvertently diagnosed while performing routine testing or testing for other diseases. A quick review of some of the protein markers reveals the possibility of such inadvertent diagnosis resulting in the practicing of the presently claimed invention. For example measuring complement factors for clotting disorders or IgM for infections may also result in the detection of the markers of the present invention.

Claim 6 and the specification have also been criticized as being unclear in the use of the term "proteome." The rejection alleges the specification and claims use multiple explanations of "proteome" some of which are contrary. This is not correct. The term "Proteome" is defined in the paragraph bridging pages 10-11. The examiner's comments

regarding page 5 of the specification are misplaced because page 5 does not appear to even mention the word "proteome."

Claim 2 and indirectly the specification are criticized as reciting Accession numbers without guidance as to the source of the Accession numbers. This is not true. Page 14, last sentence states the Accession numbers are from the NCIB non-redundant gene sequence database and the SwissProt database.

Claims 1-12 were rejected under 35 USC 112, second paragraph as being indefinite in several recitations. Claim 1 was considered indefinite in the term "protein" as being unclear which protein is being referred to. Claim 1 line 3 recites "protein" generically. For example, a cup of milk contains 8 grams of protein (the class of polypeptide compounds generally made up of any number of individual protein molecules). The other recitations of "protein" in the claims generally recite "protein markers" which refers to specific individual proteins.

Claims 2 and 3 were rejected as using improper Markush language. For the examiner's convenience, more traditional Markush language is used in amended claim 2.

Claim 6 is considered unclear in the language "proteins are increased or decreased" and comparing "levels of individual proteins". Claim 6 has been amended to better describe that individual protein abundances in the sample are being described as defined in the specification on page 8, lines 3+ and that individual protein level in the sample is being compared to a corresponding protein level in a control or another sample.

Claim 8 was considered incomplete and has been amended to read more smoothly.

Claims 11 and 12 were considered indefinite in a number of terms and as being duplicates. These claims have been amended and now avoid these problems.

Claims 1, 3, 4, 6, 9, and 10 were rejected under 35 USC 102(b) as being anticipated by Pleibner et al. The rejection is clearly incorrect with respect to claim 3 because claim 3 is

dependent on claim 2, which is not being rejected. As for the bulk of this rejection the examiner contends that Pleibner et al compares proteins from control and hypertensive rats to find alterations in the cardiac protein pattern. The rejection is respectfully traversed.

Some of the claims have been amended to recite detecting diseases other than hypertension. As such Pleibner et al provides no guidance as to what markers, if any, can be found for these other diseases. As for the claims reciting detecting protein markers for hypertension, these claims recite that the subjects are humans and that the samples are from fluids. By contrast Pleibner et al is measuring proteins in rat heart tissue. Rats are not humans and more importantly any changes in heart tissue does not necessarily imply that one will find the same change or any change at all in various protein levels in body fluids.

This position that the type of sample matters is further supported by the data in Pleibner et al and the present patent application. While the procedures are not identical, Pleibner et al reported finding only one protein spot with a statistically significant change. See page 2045, second column, lines 8-9, page 2047,Table 2, and page 2048, second column, lines 31-38 (last 7 lines). Note that Pleibner et al did not find any protein spots with a p value at $p<0.001$. The lowest found by Pleibner et al is $p=0.0032$ in table 2. By contrast, looking at plasma samples, applicants found several protein markers.

Still further, the present invention was discovered using samples from subjects having the natural disease. Pleibner et al induced an artificial state by clamping a renal artery (page 2044, section 2.1). Because the disease processes underlying hypertension are different, one would not necessarily expect to find the same or even similar results.

Accordingly, for all of the reasons above, this rejection should also be withdrawn.

In view of the amendments and comments above, the rejections have been overcome. Reconsideration, withdrawal of the rejections and early indication of allowance are respectfully requested. If any issues remain, the examiner is encouraged to telephone the undersigned.

A petition for a one-month extension of time is attached. If needed, applicants petition for an additional extension of time under the provisions of 37 CFR 1.136(a) for

sufficient time to accept this response. The commissioner hereby is authorized to charge payment of any fees under 37 CFR § 1.17, which may become due in connection with the instant application or credit any overpayment to Deposit Account No.500933.

Respectfully submitted,

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Enclosures: 1. Application Data Sheet
2. Petition for Extension of Time

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